

10/606,821

STN SEARCH 5-12-04

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L12 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2003:300856 CAPLUS
 DOCUMENT NUMBER: 138:309310
 TITLE: **Anesthetic compositions** and method
 for their administration
 INVENTOR(S): Garrett, Michael Ernest
 PATENT ASSIGNEE(S): KBIG Limited, UK
 SOURCE: PCT Int. Appl., 13 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003030862	A2	20030417	WO 2002-GB4574	20021008
WO 2003030862	A3	20030821		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: GB 2001-24071 A 20011008
 AB An inhalation anesthetic formulation comprising a suspension of the anesthetic agent in aqueous solution is disclosed.

L12 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2002:690160 CAPLUS
 DOCUMENT NUMBER: 137:218723
 TITLE: Process for evaporative removal of the dimethyl ether byproduct in the manufacture of the **sevoflurane** intermediate methyl 2,2,2-trifluoro-1-(trifluoromethyl)ethyl ether
 INVENTOR(S): Rudzinski, Ralph; Lessor, Ralph
 PATENT ASSIGNEE(S): Baxter International, Inc., USA
 SOURCE: U.S., 6 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6448451	B1	20020910	US 2001-874346	20010605
WO 2002098831	A2	20021212	WO 2002-US14096	20020502
WO 2002098831	A3	20031127		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,				

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UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
EP 1392631 A2 20040303 EP 2002-736649 20020502
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: US 2001-874346 A 20010605
WO 2002-US14096 W 20020502

AB A process for purifying Me 2,2,2-trifluoro-1-(trifluoromethyl)ethyl ether comprises: passing a **composition** containing Me 2,2,2-trifluoro-1-(trifluoromethyl)ethyl ether and di-Me ether through an evaporation zone; evaporating the di-Me ether by passing a gas stream through the **compon** .; and removing the gas comprising di-Me ether from the **composition** Me 2,2,2-trifluoro-1-(trifluoromethyl)ethyl ether is an intermediate in the manufacture of the inhalation anesthetic **sevoflurane**.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:429551 CAPLUS

DOCUMENT NUMBER: 136:395980

TITLE: Xenon as NMDA antagonist, and use as a neuroprotectant and/or as an inhibitor of synaptic plasticity and in the treatment of neuropathic pain

INVENTOR(S): Franks, Nicholas Peter; Maze, Mervyn

PATENT ASSIGNEE(S): Protexon Limited, UK

SOURCE: U.S. Pat. Appl. Publ., 28 pp., Cont.-in-part of U.S. Ser. No. 857,146.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002068764	A1	20020606	US 2001-881178	20010614
US 6653354	B2	20031125		
US 6274633	B1	20010814	US 1999-378806	19990823
WO 2001008692	A1	20010208	WO 2000-GB2896	20000728

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 1999-17822 A 19990729
US 1999-378806 A2 19990823
WO 2000-GB2896 A2 20000728
US 2001-857146 A2 20010531

AB The invention provides the use of xenon as a neuroprotectant and/or as an inhibitor of synaptic plasticity. In a preferred aspect, the xenon acts as an NMDA antagonist. The invention also provides a method of reducing the level of activation of the NMDA receptors in a mammal, the method comprising modulating the activity of the NMDA receptor by administering to the mammal a therapeutically effective amount of xenon, wherein said reduction achieves neuroprotection and/or an inhibition of synaptic

plasticity. A further embodiment of the invention provides a pharmaceutical **composition** for providing neuroprotection and/or inhibition of synaptic plasticity, together with a process for the preparation thereof. Another aspect of the invention relates to a pharmaceutical **composition** suitable for providing neuroprotection, inhibiting synaptic plasticity or relieving neuropathic pain, said **composition** comprising xenon and a GABAergic agent admixed with a pharmaceutically acceptable carrier, excipient or diluent.

L12 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:726282 CAPLUS

DOCUMENT NUMBER: 132:30291

TITLE: A model-based dependence of the human tissue/blood partition coefficients of chemicals on lipophilicity and tissue **composition**

AUTHOR(S): Balaz, Stefan; Lukacova, Viera

CORPORATE SOURCE: College of Pharmacy, Department of Pharmaceutical Sciences, North Dakota State University, Fargo, ND, 58105, USA

SOURCE: Quantitative Structure-Activity Relationships (1999), 18(4), 361-368

CODEN: QSARDI; ISSN: 0931-8771

PUBLISHER: Wiley-VCH Verlag GmbH

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Partitioning of up to thirty-six nonionizable chems. between seven tissues (fat, liver, brain, kidney, muscle, lung, heart) and blood in humans was modeled using membrane accumulation, protein binding, and distribution in the aqueous phases as relevant processes. The extent of membrane accumulation and protein binding of individual compds. was described as the Collander-type function of their lipophilicity expressed by the 1-octanol/**water** partition coeffs. The resulting model-based expression described satisfactorily the tissue/blood partition coeffs. as a nonlinear function of lipophilicity and tissue **composition** (a standard content of lipids, proteins, and **water**). The calibrated model is suitable for prediction of the tissue/blood partition coeffs. for non-amphiphilic nonionizable chems. with the 1-octanol/**water** partition coeffs. varying between 0.01 and 100,000, i.e. practically in the whole range for which equilibrium tissue/blood distribution can be used in physiol. based pharmacokinetic models.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:60446 CAPLUS

DOCUMENT NUMBER: 130:281720

TITLE: Ureas and amides as dipolar aprotic solvents in highly basic media. The dependence of kinetic basicity on solvent **composition**

AUTHOR(S): Kankaanpera, Alpo; Scharlin, Pirketta; Kuusisto, Ilona; Kallio, Riitta; Bernoulli, Emma

CORPORATE SOURCE: Department of Chemistry, University of Turku, Turku, FIN-20014, Finland

SOURCE: Journal of the Chemical Society, Perkin Transactions 2: Physical Organic Chemistry (1999), (2), 169-174

CODEN: JCPKBH; ISSN: 0300-9580

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The basicity of dipolar aprotic solvent-**water**-HO- systems with amides and ureas as the organic component has been studied kinetically

because previous information is not available, excluding some H- values measured for aqueous DMF and tetramethylurea (TMU). It was found that the increase in basicity with the mole fraction of organic component is at least of the same magnitude as in aqueous DMSO. For instance, in the detritiation of chloroform-t the slopes of the plots $\log(k_2/\text{mol}^{-1} \text{ dm}^3 \text{ s}^{-1})$ vs. $x(\text{urea})$ varied between 11.4-14.6 (as compared to 11.0 in aqueous DMSO) when TMU and cyclic ureas, 1,3-dimethylimidazolidin-2-one (DMI) and 1,3-dimethyl-3,4,5,6-tetrahydropyrimidin-2(1H)one (DMPU), were used as the organic component in solvent mixture. In aqueous TMU acidity functions H-

were

extrapolated from kinetic results using linear free energy correlations. Agreement with literature values was evident. This method was also used to extrapolate the H- values in aqueous DMPU. On the basis of present work aqueous ureas can be recommended as solvents in highly basic media. The utility of amides, DMF and dimethylacetamide, is limited by their instability in basic **water** solns.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LI2 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:527197 CAPLUS

DOCUMENT NUMBER: 129:166218

TITLE: Fluoroether **compositions** and methods for inhibiting their degradation in the presence of a Lewis acid

INVENTOR(S): Bieniarz, Christopher; Chang, Steve H.; Cromack, Keith R.; Huang, Shuyen L.; Kawai, Toshikazu; Kobayashi, Manami; Loffredo, David; Raghavan, Rajagopalan; Speicher, Earl R.; Stelmach, Honorate A.

PATENT ASSIGNEE(S): Abbott Laboratories, USA

SOURCE: PCT Int. Appl., 25 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9832430	A1	19980730	WO 1998-US1376	19980123
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW			
RW:	AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
US 5990176	A	19991123	US 1997-789679	19970127
ZA 9800418	A	19990420	ZA 1998-418	19980119
CA 2352597	AA	19980730	CA 1998-2352597	19980123
AU 9859300	A1	19980818	AU 1998-59300	19980123
AU 726733	B2	20001116		
EP 967975	A1	20000105	EP 1998-902707	19980123
EP 967975	B1	20010613		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO			
BR 9806996	A	20000314	BR 1998-6996	19980123
JP 2000510159	T2	20000808	JP 1998-532168	19980123
JP 3183520	B2	20010709		
NZ 335994	A	20000825	NZ 1998-335994	19980123
CA 2278133	C	20010626	CA 1998-2278133	19980123

JP 2001187729	A2	20010710	JP 2000-349024	19980123
EP 1114641	A2	20010711	EP 2001-107733	19980123
EP 1114641	A3	20030528		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI, RO				
PT 967975	T	20011130	PT 1998-902707	19980123
ES 2170474	T3	20020801	ES 1998-902707	19980123
NO 9903606	A	19990924	NO 1999-3606	19990723
US 6288127	B1	20010911	US 1999-447853	19991123
GR 3036190	T3	20011031	GR 2001-401038	20010706
US 2002016373	A1	20020207	US 2001-924573	20010808
US 6444859	B2	20020903		
US 2003130359	A1	20030710	US 2002-190271	20020703
US 6677492	B2	20040113		
US 2004048932	A1	20040311	US 2003-606821	20030626

PRIORITY APPLN. INFO.:

US 1997-789679	A	19970127
CA 1998-2278133	A3	19980123
EP 1998-902707	A3	19980123
JP 1998-532168	A3	19980123
WO 1998-US1376	W	19980123
US 1999-447853	A1	19991123
US 2001-924573	A1	20010808
US 2002-190271	A1	20020703

AB The present invention relates to an **anesthetic composition** containing an anhydrous **fluoroether compound** and a physiologically acceptable **Lewis acid inhibitor** (e.g. **water**, **BHT**, **methylparaben**, **propofol**, **thymol**). This **composition** exhibits improved stability and does not degrade in the presence of a Lewis acid. An example is given showing that the degradation of **sevoflurane** in activated Type III amber glass bottles was greatly inhibited by treating the activated glass surface with **water** saturated **sevoflurane** prior to heating.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1994:400260 CAPLUS

DOCUMENT NUMBER: 121:260

TITLE: Inhibitory effects of **propofol** on cytochrome P450 activities in rat hepatic microsomes

AUTHOR(S): Baker, Max T.; Chadam, Maria V.; Ronnenberg, William C. Jr.

CORPORATE SOURCE: Dep. Anesth., Univ. Iowa, Iowa City, IA, 52242, USA

SOURCE: Anesthesia & Analgesia (Baltimore, MD, United States) (1993), 76(4), 817-21

CODEN: AACRAT; ISSN: 0003-2999

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effects of **propofol** on cytochrome P 450 activity in rat hepatic microsomes were evaluated to determine the potential influence of this anesthetic on the metabolism of coadministered agents. In microsomes from untreated and isoniazid-treated rats, **propofol** was a weak inhibitor of **enflurane** metabolism, inhibiting activity only at 0.35 mM **propofol**. In contrast, toluene, a related compound, at concns. as low as 0.025 mM, effectively impaired **enflurane** defluorination in microsomes from untreated, and isoniazid- and phenobarbital-treated rats. **Propofol**, in contrast to toluene, was an effective inhibitor of benzphetamine demethylation, as it inhibited this activity at concns. as low as 0.025 mM in microsomes from phenobarbital-treated rats. In microsomes from phenobarbital-treated rats, **propofol** potentially inhibited the metabolism of aniline.

Sixty-four percent inhibition was achieved at 0.03 mM **propofol**, whereas toluene had no effect at 1 mM. These data demonstrate that **propofol** does not effectively inhibit **enflurane** metabolism by the isoniazid-inducible cytochrome P450IIE1 but effectively impairs activities of the phenobarbital-inducible cytochrome P 450 isoenzymes.

L12 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1994:261262 CAPLUS

DOCUMENT NUMBER: 120:261262

TITLE: The effects of **propofol** and **enflurane** on single calcium channel currents of guinea pig isolated ventricular myocytes

AUTHOR(S): Takahashi, H.; Puttick, R. M.; Terrar, D. A.

CORPORATE SOURCE: Univ. Dep. Pharmacol., Oxford, OX1 3QT, UK

SOURCE: British Journal of Pharmacology (1994), 111(4), 1147-53

CODEN: BJPCBM; ISSN: 0007-1188

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effects of the anesthetics, **propofol** (100 μ M) and **enflurane** (3%, 1.46 mM), on single L type calcium channel currents were investigated in single myocytes isolated from guinea-pig ventricles. Channel activity was recorded from membrane patches by use of the 'cell-attached' patch-clamp technique (pipet solution containing 110 mM BaCl₂,

5

μ M Bay K 8644, 5 μ M HEPES, pH 7.4; temperature 36°C). Channel conductance was calculated from the slope of the relationship between single channel current and membrane potential during step depolarizations to activate the channel over a range of approx. -20 to +20 mV. Neither **propofol** (6 cells) nor **enflurane** (7 cells) caused any significant reduction in channel conductance. Both **propofol** (7 cells) and **enflurane** (9 cells) decreased the probability of the channel being open during depolarizations to +10 mV (measured from histograms of the fraction of time spent by the channel at different current levels, taking areas under the Gaussian curves fitted to the open and closed components of the distributions to represent the proportion of time spent in the two states). A fraction of the current traces showed no detectable channel openings in response to step depolarizations to +10 mV. Both **propofol** and **enflurane** significantly increased the fraction of silent traces. Transitions across a threshold halfway between the open and closed levels were used to define periods spent in the open and closed states. Both **propofol** (7 cells) and **enflurane** (9 cells) reduced the mean open times and increased the mean closed times of the calcium channel. Histograms were plotted showing the distributions of times spent by the channels in the open and closed states. Two exponentials were fitted to the open and closed time distributions. Both **propofol** (7 cells) and **enflurane** (9 cells) shortened both time constants, fitted to the open times and lengthened both time constants, fitted to the closed times. It is concluded that both **propofol** and **enflurane** appear to alter the kinetics of opening and closing of calcium channels to favor shut channels without altering channel conductance. This effect would be expected to result in a reduction of the macroscopic calcium current and thus contribute to the neg. inotropic action of these anesthetics.

L12 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1993:32848 CAPLUS

DOCUMENT NUMBER: 118:32848

TITLE: General anesthetics potentiate γ -aminobutyric acid actions on γ -aminobutyric acidA receptors expressed by *Xenopus* oocytes: lack of involvement of

intracellular calcium
 AUTHOR(S): Lin, Lie Huey; Chen, Longtang L.; Zirrolli, Joseph A.; Harris, R. Adron
 CORPORATE SOURCE: Health Sci. Cent., Univ. Colorado, Denver, CO, USA
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (1992), 263(2), 569-78
 CODEN: JPETAB; ISSN: 0022-3565
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Potentiation of the γ -aminobutyric acid (GABAA) receptor-gated Cl⁻ channel response has been suggested to be a primary action of some anesthetic agents. Whether the GABAA receptor is a target site common for general anesthetics that are chemical and structurally diverse was examined. This hypothesis was tested in *Xenopus* oocytes expressing mouse cortical mRNA, and GABA-activated Cl⁻ currents were measured using two-electrode voltage clamping. General anesthetics, including inhalational (halothane, di-Et ether, **enflurane** and **isoflurane**), i.v. (3 α -hydroxy-5 α -dihydroprogesterone, ketamine and **propofol**) and alc. (pentanol) anesthetics, enhanced GABA-induced currents by 56 to 1089% at concns. that were clin. relevant. The results suggest that potentiation of the GABAA receptor/channel response may be a common action for anesthetic agents. Moreover, anesthetic effects were dependent on GABA concns.; the enhancement was marked with low GABA concns. and was exponentially decreased as the GABA concentration increased. Also, anesthetic effects were dependent on anesthetic concns. The apparent EC50 of halothane was found to be similar to the anesthetic ED50. The role of intracellular Ca²⁺ in mediating anesthetic enhancement of the GABA current was also examined. It was found that intracellular injection of the Ca²⁺ chelator, EGTA, did not change the enhancement by anesthetics. In addition, these anesthetics alone did not produce significant currents, suggesting that the Ca²⁺-dependent Cl⁻ current was not activated by these anesthetics per se. Thus, it was found that diverse anesthetics potentiate GABA-induced Cl⁻ currents, but this action is not mediated by a release of intracellular Ca²⁺.

L12 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1980:581797 CAPLUS

DOCUMENT NUMBER: 93:181797

TITLE: Intrinsic differences in the perturbing ability of alkanols in bilayer: action of phospholipase A2 on the alkanol-modified phospholipid bilayer

AUTHOR(S): Upreti, Girish C.; Rainier, Shirley; Jain, Mahendra K.

CORPORATE SOURCE: Dep. Chem., Univ. Delaware, Newark, DE, 19711, USA

SOURCE: Journal of Membrane Biology (1980), 55(2), 97-112

CODEN: JMBBBO; ISSN: 0022-2631

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The kinetic parameters for the steady-state rate of hydrolysis of egg phosphatidylcholine in multilamellar vesicles by bee venom phospholipase A2 are measured in the presence of 27 alkanols and several organic solvents. In general, small nonpolar solutes like **enflurane**, THF, benzene, chloroform and di-Et ether do not promote the hydrolysis of multilamellar vesicles. The rate of hydrolysis shows a biphasic dependence upon the alkanol concentration for all higher (C5-C9) alcs. examined, i.e., an optimal rate

of hydrolysis is observed at a characteristic concentration for each alc. The alkanol to lipid mole ratio (D/L ratio) in the bilayer at the peak activating concentration of an alkanol was computed from its bilayer/**water** partition coefficient. The branched-chain alcs. induce peak activation of hydrolysis at lower D/L ratios in the bilayer than the corresponding straight chain analogs. Similarly, the longer chain

n-alkanols at peak activating concentration have a lower D/L ratio than the corresponding lower alcs. Both the K_m and V_{max} for phosphatidylcholine increase as a function of the chain length of activating alc. These kinetic parameters also depend upon the position of the substituents on the activating alcs. Both the D/L ratio and V_{max} for an alc. change with the cross-sectional area of the activating alc. across its long axis: alcs. with a more asym. cross-section exhibit higher V_{max} and a lower D/L ratio. Such correlations of V_{max} and D/L ratio with the mol. parameters of the alkanols are interpreted to suggest that the accessibility of the substrate mol. in the bilayer to the phospholipase is modulated by the free space introduced by the alkanols in the bilayer. Effects of tetradecane derivs. and A2C (a membrane fluidizing agent) on the phase transition characteristics of dipalmitoylphosphatidylcholine bilayers, and their susceptibility to phospholipase A2 from bee venom and pig pancreas are also reported. These solutes cause a broadening of the transition profile and reduce the size of the cooperative unit and the enthalpy of transition. These effects depend upon the mole fraction of a solute in the bilayer; however, equal concns. of these solutes do not induce equal response. Susceptibility of the modified bilayers to phospholipase A2 depends not only upon the structure of the solute but also upon the source of the enzyme. The activity of the membrane-bound enzyme is modulated to different extents by different solutes, and the bilayer perturbing ability of these solutes may be related to the asymmetry of their cross-sectional area and to the free space introduced by the alkanols in a bilayer.

L12 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1978:58557 CAPLUS

DOCUMENT NUMBER: 88:58557

TITLE: The effect in vitro of volatile anesthetics on the activity of cholinesterases

AUTHOR(S): Braswell, L. M.; Kitz, R. J.

CORPORATE SOURCE: Harvard Med. Sch., Massachusetts Gen. Hosp., Boston, MA, USA

SOURCE: Journal of Neurochemistry (1977), 29(4), 665-71
CODEN: JONRA9; ISSN: 0022-3042

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Purified human serum cholinesterase (EC 3.1.1.8) [9001-08-5] was insensitive to saturated solns. of 8 volatile anesthetics (ether [60-29-7], **methoxyflurane** [76-38-0], CHCl_3 [67-66-3], trichloroethylene [79-01-6], fluroxene [406-90-6], CF_3CHClBr [151-67-7], **enflurane** [13838-16-9], and **isoflurane** [26675-46-7]); purified dog brain and human erythrocyte acetylcholinesterase (EC 3.1.1.7) (I) [9000-81-1] was reversibly and dose-dependently inhibited by all the anesthetics in concns. greater than those used clin. The inhibition was of the mixed type except for the ether-erythrocyte I interaction where the inhibition was competitive. Ether and **methoxyflurane** depressed I activity the most and **isoflurane** and **enflurane** the least. The concns. of ether, **methoxyflurane**, CHCl_3 , trichloroethylene, and CF_3CHClBr in the gas phase necessary for 50% inhibition of I activity correlated with the resp. water-gas partition coeffs. Thus the in vitro effect of volatile anesthetics on cholinesterase activity is variable and may be unrelated to anesthetic potency in vivo; anesthetic-active site interactions were discussed.

L12 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1971:21642 CAPLUS

DOCUMENT NUMBER: 74:21642

TITLE: Determination of volatile organic anesthetics in blood, gases, tissues, and lipids. Partition coefficients

10/606,821

AUTHOR(S): Lowe, Harry J.; Hagler, K.
CORPORATE SOURCE: Med. Sch., Univ. of Chicago, Chicago, IL, USA
SOURCE: Gas Chromatogr. Biol. Med., Ciba Found. Symp. (1969),
86-112. Editor(s): Porter, Ruth. J. and A. Churchill
Ltd.: London, Engl.
CODEN: 17ZTAE
DOCUMENT TYPE: Conference
LANGUAGE: English

AB The **water**-gas and blood-gas partition coeffs. of cyclopropane, trifluoroethylene, CHCl_3 , vinyl ether, divinyl ether, Et_2O , trichloroethylene, halothane (I), and **methoxyflurane** (II) were determined (curves shown) in the range $10-40^\circ$ and as a function of the blood hematocrit. Both partition coeffs. of cyclopropane increased with decreasing gas concentration. Anesthetic partition coeffs. in human fat, cephalin, lecithin, sphingomyelin, and cholesterol were determined at $10-40^\circ$. In this temperature range, the enthalpy of soln, of each anesthetic in each lipid was constant. The partition coeffs. determined were used

to calculate the anesthetic partition coeffs. in human brain and calf tissues from the known lipid **composition** of the tissues. The inverse linear logarithmic relation between anesthetic potency and solubility in phospholipid and brain tissue supported the lipid theory of anesthesia. Tests with I showed that blood flow may be as high as 100 ml/kg for mesenteric fat but only 18 ml/kg for s.c. fat. For II, blood levels within 10% of predicted values were obtained, since II does not significantly disturb blood flow to any organ. Liver microsomes degraded I. Tests with I tagged with ^{82}Br showed that neutron irradiation caused breakdown of I to various dibromo compds. and other products. Such impurities must be removed before I can be used in man.

=> d his

(FILE 'HOME' ENTERED AT 08:40:03 ON 12 MAY 2004)

FILE 'CAPLUS' ENTERED AT 08:40:09 ON 12 MAY 2004

L1 2 S FLUOROETHER COMPOUND?
L2 90 S ANESTHETIC COMPOSITION?
L3 6453 S SEVOFLURANE OR ENFLURANE OR ISOFLURANE OR METHOXYFLURANE OR D
L4 6454 S L1 OR L3
L5 3 S LEWIS ACID INHIBITOR?
L6 2144034 S WATER OR BUTYLATED HYDROXYTOLUENE OR METHYLPARABEN OR PROPYLP
L7 2144036 S L5 OR L6
L8 834 S L4 AND L7
L9 0 S L8/THU
L10 12 S L8 AND COMPOSITIO?
L11 2 S L8 AND L2
L12 12 S L10 OR L11

=>

PALM INTRANET

Day : Wednesday

Date: 5/12/2004

Time: 08:35:32

Inventor Name Search Result

Your Search was:

Last Name = BIENIARZ

First Name = CHRISTOPHER

Application#	Patent#	Status	Date Filed	Title	Inventor Name 43
<u>60531721</u>	Not Issued	019	12/22/2003	MICROWAVE MEDIATED SYNTHESIS OF NUCLEIC ACID PROBES	BIENIARZ, CHRISTOPHER
<u>60482596</u>	Not Issued	020	06/24/2003	ENZYME-CATALYZED METAL DEPOSITION FOR THE ENHANCED IN SITU DETECTION OF IMMUNOHISTOCHEMICAL EPITOPES AND NUCLEIC ACID SEQUENCES	BIENIARZ, CHRISTOPHER
<u>60364210</u>	Not Issued	159	03/14/2002	COMPOUNDS FOR ANESTHESIA AND SEDATION	BIENIARZ, CHRISTOPHER
<u>10606821</u>	Not Issued	030	06/26/2003	FLUOROETHER COMPOSITIONS AND METHODS FOR INHIBITING THEIR DEGRADATION IN THE PRESENCE OF A LEWIS ACID	BIENIARZ, CHRISTOPHER
<u>10190271</u>	<u>6677492</u>	150	07/03/2002	FLUOROETHER COMPOSITIONS AND METHODS FOR INHIBITING THEIR DEGRADATION IN THE PRESENCE OF A LEWIS ACID	BIENIARZ, CHRISTOPHER
<u>09924573</u>	<u>6444859</u>	150	08/08/2001	FLUOROETHER COMPOSITIONS AND METHODS FOR INHIBITING THEIR DEGRADATION IN THE PRESENCE OF A LEWIS ACID	BIENIARZ, CHRISTOPHER
<u>09587421</u>	<u>6303831</u>	150	06/01/2000	SYNTHETIC METHOD FOR FLUOROMETHYLATION OF HALOGENATED ALCOHOLS	BIENIARZ, CHRISTOPHER

<u>09587417</u>	<u>6271422</u>	150	06/01/2000	METHOD FOR FLUOROMETHYLATION OF ALCOHOLS VIA HALOGENATIVE DECARBOXYLATION	BIENIARZ, CHRISTOPHER
<u>09587414</u>	<u>6245949</u>	150	06/01/2000	SYNTHETIC METHOD FOR THE FLUOROMETHYLATION OF ALCOHOLS	BIENIARZ, CHRISTOPHER
<u>09498388</u>	<u>6160153</u>	150	02/03/2000	PHOSPHATASE ACTIVATED CROSSLINKING CONJUGATING AND REDUCING AGENTS; METHODS OF USING SUCH AGENTS; AND REAGENTS COMPRISING PHOSPHATASE ACTIVATED CROSSLINKING AND CONJUGATING	BIENIARZ, CHRISTOPHER
<u>09447853</u>	<u>6288127</u>	150	11/23/1999	FLUOROETHER COMPOSITIONS AND METHODS FOR INHIBITING THEIR DEGRADATION IN THE PRESENCE OF A LEWIS ACID	BIENIARZ, CHRISTOPHER
<u>09444478</u>	<u>6503528</u>	150	11/19/1999	POLYMERIC COMPOSITIONS AND A METHOD OF MAKING THE SAME	BIENIARZ, CHRISTOPHER
<u>09280794</u>	<u>6100434</u>	150	03/26/1999	METHOD FOR SYNTHESIZING SEVOFLURANE AND AN INTERMEDIATE THEREOF	BIENIARZ, CHRISTOPHER
<u>09040702</u>	Not Issued	163	03/18/1998	FLUORESCENT POLYMER LABELED CONJUGATES AND INTERMEDIATES	BIENIARZ, CHRISTOPHER
<u>08848784</u>	Not Issued	161	05/01/1997	FLUORESCENT POLYMER LABELED CONJUGATES AND INTERMEDIATES	BIENIARZ, CHRISTOPHER
<u>08789679</u>	<u>5990176</u>	150	01/27/1997	FLUOROETHER COMPOSITIONS AND METHODS FOR INHIBITING THEIR DEGRADATION IN THE PRESENCE OF A LEWIS ACID	BIENIARZ, CHRISTOPHER
<u>08734157</u>	<u>6015902</u>	150	10/21/1996	INTERCALATORS HAVING AFFINITY FOR DNA AND METHODS OF USE	BIENIARZ, CHRISTOPHER
<u>08657695</u>	<u>6057429</u>	150	05/29/1996	PHOSPHATASE ACTIVATED	BIENIARZ,

				CROSSLINKING, CONJUGATING AND REDUCING AGENTS; METHODS OF USING SUCH AGENTS; AND REAGENTS COMPRISING PHOSPHATASE ACTIVATED CROSSLINKING AND CONJUGATING AGENTS	CHRISTOPHER
<u>08655067</u>	<u>5789219</u>	150	05/29/1996	PHOSPHATASE ACTIVATED CROSSLINKING CONJUGATING AND REDUCING AGENTS; METHODS OF USING SUCH AGENTS; AND REAGENTS COMPRISING PHOSPHATASE ACTIVATED CROSSLINKING AND CONJUGATING AGENTS	BIENIARZ , CHRISTOPHER
<u>08595092</u>	<u>5994143</u>	150	02/01/1996	POLYMERIC FLUOROPHORES ENHANCED BY MOIETIES PROVIDING A HYDROPHOBIC AND CONFORMATIONALLY RESTRICTIVE MICROENVIRONMENT	BIENIARZ , CHRISTOPHER
<u>08464185</u>	<u>5599932</u>	150	06/05/1995	INTERCALATORS HAVING AFFINITY FOR DNA AND METHODS OF USE	BIENIARZ , CHRISTOPHER
<u>08463324</u>	<u>5808077</u>	150	06/05/1995	INTERCALATORS HAVING AFFINITY FOR DNA AND METHODS OF USE	BIENIARZ , CHRISTOPHER
<u>08349167</u>	<u>5736624</u>	150	12/02/1994	PHOSPHATASE ACTIVATED CROSSLINKING, CONJUGATING AND REDUCING AGENTS; METHODS OF USING SUCH AGENTS; AND REAGENTS COMPRISING PHOSPHATASE ACTIVATED CROSSLINKING AND CONJUGATING AGENTS	BIENIARZ , CHRISTOPHER
<u>08324004</u>	<u>5661040</u>	150	10/14/1994	FLUORESCENT POLYMER LABELED CONJUGATES AND INTERMEDIATES	BIENIARZ , CHRISTOPHER
<u>08270285</u>	Not Issued	168	07/11/1994	FLUORESCENT POLYMER LABELED CONJUGATES AND	BIENIARZ , CHRISTOPHER

				INTERMEDIATES	
<u>08268043</u>	<u>5582984</u>	150	06/29/1994	METHODS OF USE OF PHENANTHRIDIUM DNA INTERCALATORS FOR FLUORESCENCE DETECTION	BIENIARZ , CHRISTOPHER
<u>08265342</u>	Not Issued	166	06/23/1994	INTERCALATOR HAVING AFFINITY FOR DNA AND METHODS OF USE	BIENIARZ , CHRISTOPHER
<u>08091149</u>	Not Issued	168	07/13/1993	FLUORESCENT POLYMER LABELED CONJUGATES AND INTERMEDIATES	BIENIARZ , CHRISTOPHER
<u>08086285</u>	Not Issued	166	06/30/1993	INTERCALATORS HAVING AFFINITY FOR DNA AND METHODS OF USE	BIENIARZ , CHRISTOPHER
<u>07999181</u>	<u>5380873</u>	150	12/22/1992	HOMOBIFUNCTIONAL AGENTS FOR COUPLING ENZYMES AND THE LIKE TO ANTIBODIES AND THE LIKE	BIENIARZ , CHRISTOPHER
<u>07827669</u>	<u>5272260</u>	150	01/29/1992	REAGENTS AND METHODS FOR THE DETERMINATION OF GLYCOHYDROLYTIC ENZYMES	BIENIARZ , CHRISTOPHER
<u>07753247</u>	Not Issued	161	08/30/1991	CHROMOGENIC CEPHALOSPORIN DERIVATIVES, PREPARATION USE IN ASSAYS AND OTHER BIOLOGICAL APPLICATIONS	BIENIARZ , CHRISTOPHER
<u>07752310</u>	Not Issued	161	08/30/1991	FLUOROGENIC CEPHALOSPORIN DERIVATIVES, PREPARATION, AND USE IN ASSAYS AND OTHER BIOLOGICAL APPLICATIONS	BIENIARZ , CHRISTOPHER
<u>07624169</u>	<u>5191066</u>	150	12/07/1990	SITE-SPECIFIC CONJUGATION OF IMMUNOGLOBULINS AND DETECTABLE LABELS	BIENIARZ , CHRISTOPHER
<u>07600795</u>	Not Issued	166	10/22/1990	HOMOBIFUNCTIONAL AGENTS FOR COUPLING ENZYMES AND THE LIKE TO ANTI- BODIES AND THE LIKE	BIENIARZ , CHRISTOPHER

<u>07402013</u>	<u>5063109</u>	150	09/01/1989	COVALENT ATTACHMENT OF ANTIBODIES AND ANTIGENS TO SOLID PHASES USING EXTENDED LENGTH HETEROBIFUNCTIONAL COUPLING AGENTS	BIENIARZ , CHRISTOPHER
<u>07402012</u>	<u>5053520</u>	150	09/01/1989	HETEROBIFUNCTIONAL MALEIMIDO CONTAINING COUPLING AGENTS	BIENIARZ , CHRISTOPHER
<u>07367151</u>	<u>4970074</u>	150	07/24/1989	FLUOROPHORES FOR ENCAPSULATION INTO LIPOSOMES	BIENIARZ , CHRISTOPHER
<u>07298098</u>	<u>4978613</u>	150	01/17/1989	BETA-LACTAMASE ASSAY EMPLOYING CHROMOGENIC PRECIPITATING SUBSTRATES	BIENIARZ , CHRISTOPHER
<u>07254288</u>	<u>5002883</u>	150	10/11/1988	COVALENT ATTACHMENT OF ANTIBODIES AND ANTIGENS TO SOLID PHASES USING EXTENDED LENGTH HETEROBIFUNCTIONAL COUPLING AGENTS	BIENIARZ , CHRISTOPHER
<u>07246971</u>	<u>4994385</u>	150	09/22/1988	HETEROBIFUNCTIONAL COUPLING AGENTS	BIENIARZ , CHRISTOPHER
<u>07114930</u>	Not Issued	161	10/30/1987	HETEROBIFUNCTIONAL COUPLING AGENTS	BIENIARZ , CHRISTOPHER
<u>07067833</u>	<u>4912208</u>	150	06/29/1987	FLUOROPHORES FOR ENCAPSULATION INTO LIPOSOMES	BIENIARZ , CHRISTOPHER

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